Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 119-138 are pending in this application and are rejected/objected to on various grounds. Claims 119-121, 127-128 and 132-134 have been canceled without prejudice or disclaimer towards claiming their subject matter in subsequent continuation or divisional applications. Accordingly, Claims 122-126 and 129-131 and 135-138 are now pending in this application. The pending claims have been amended to remove references to Figures and for clarity. The rejections to the presently pending claims are respectfully traversed.

Formal Matters

The title of the invention has been amended to more particularly claim what the Applicants considers as their invention.

Information Disclosure Statement

Applicants will shortly file an IDS identifying the sequences from the Blast search by author, dates, etc.

Priority Determination

Applicants rely on the gene amplification assay for patentable utility which was first disclosed in U.S. Provisional Application 60/141,037, filed June 23, 1999, priority to which has been claimed in this application. Hence, Applicants should be entitled to at least an effective filing date of **June 23, 1999.**

Claim Rejections – 35 USC §101 and 112, First paragraph- Enablement

Claims 119-138 are rejected under 35 U.S.C. §101 for not being supported by either a specific, substantial and credible asserted utility or a well established utility.

Claims 119-138 are further rejected under 35 U.S.C. §112, first paragraph allegedly since the claimed invention is not supported by either a specific, substantial and credible asserted utility or well established utility, one skilled in the art clearly would not know how to use the claimed invention.

The Examiner asserts that "there is no disclosure of any disease or condition or analytical assay that could be performed using the claimed nucleic acids". For the reasons outlined below, Applicants respectfully traverse.

Applicants submit that the cancellation of claims 119-121, 127-128 and 132-134, without prejudice or disclaimer, renders this rejection moot to these claims. Further, without acquiescing to the propriety of this rejection, Applicants have amended claims 122-123 and 125-126 to recite a functional recitation: "wherein the nucleic acid encoding said polypeptide is amplified in lung tumors."

As mentioned above under the section of priority, Applicants rely on the data presented in the gene amplification assay for patentable utility for this case. As the Examiner has noted, PRO809 gene is amplified 1.05 -1.61, that is, **2.070 to 3.053** fold amplification, which is significant, according to the attached Declaration by Audrey Goddard, Ph.D., an expert in the gene amplification assay and co-inventor of this application.

Further, regarding the Examiner's rejection that there is a lack of correction of gene amplification data based on aneuploidy, Applicants submit that, as rightly noted by the Examiner and the Sen article, aneuploid tissues are **cancerous or pre-cancerous**. The present invention is directed to nucleic acids useful in the detection of cancer, irrespective of the mechanism by which gene amplification occurs. Even if the presence aneuploid cells or tissues were to predict a propensity towards cancer, the instant nucleic acids are still useful as diagnostic tools. Applicants have further included a declaration by Avi Ashkenazi, Ph.D., a co-inventor of this application, who says that:

> "An increase in gene copy number can result not only from intrachromosomal changes but also from chromosomal aneuploidy. It is important to understand that detection of gene amplification can be used for cancer diagnosis even if the determination includes measurement of chromosomal aneuploidy. Indeed, as long as a significant difference relative to normal tissue is detected, it is irrelevant if the signal originates from an increase in the number of gene copies per chromosome and/or an abnormal number of chromosomes."

Therefore, a person of skill in the art would certainly consider the gene amplification results as significant and diagnostic for lung tumors.

Thus, Applicants believe that this rejection under 35 U.S.C. §101 and 112, first paragraph should be withdrawn.

Claim Rejections – 35 USC § 112, first paragraph-Written description

Claims 119-124, 127-128 and 132-138 are rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have canceled claims 119-121, 127-128 and 132-134, without prejudice or disclaimer, and hence this rejection is moot with respect to these claims. Without acquiescing to the propriety of this rejection, Applicants have amended the pending claims to recite a functional recitation: "wherein the nucleic acid encoding said polypeptide is amplified in lung tumors." Further, Example 14 of the Written Description Guidelines issued by the U.S. Patent Office which clearly states that "protein variants meets the requirements of 35 U.S.C.§112 first paragraph as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins is routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the specified functional activity and at least 95% sequence identity to the reference sequence". Based on these guidelines, Applicants submit that the instant specification evidences the actual reduction to practice of a full-length native human PRO809 polypeptide of SEQ ID NO: 223, with or without its signal sequence and of the nucleic acid of SEQ ID NO: 222. In addition, the specification provides detailed description about the cloning of variants (see, e.g. pages 154-155 and 196-201), and describes the gene amplification assay for testing nucleic acids in a PCR based assay. Thus, Applicants submit that the genus of nucleic acids that code for the polypeptide of SEQ ID NO: 223 or variants of nucleic acid of SEQ ID NO: 222 with 95% similarity and further, which possess the functional property that it is "amplified in a lung tumors" would encompass a genus that meets the requirements of 35 U.S. C. §112, first paragraph as providing adequate written description.

Thus, one of skill in the art would know that Applicants had possession of the invention, as described in the instantly amended claims, and therefore request that this rejection be withdrawn.

Claim Rejections – 35 USC § 112, second paragraph

Claims 119-138 were rejected under 35 U.S.C. §112, second paragraph for being indefinite.

Without acquiescing to the propriety of this rejection, Applicants have canceled references to "the extracellular domain" and "the extracellular domain....lacking its associated signal sequence" in the pending claims. Accordingly, this rejection should be withdrawn.

Deposit Requirement

Claims 119-138 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and/or use the invention.

The specification, as amended, includes the statement as specified by the Examiner and hence, is compliant with the requirements of the Budapest Treaty. Therefore, this rejection should be withdrawn.

Claim Rejections – 35 USC § 102(b)

Claims 119-138 are rejected under 35 U.S.C. 102(b) as being anticipated by clone H74302 isolated by Hillier *et al.* (1995).

H74302 (582 nucleotides) has 58.66% similarity to SEQ ID NO: 222 defined in the claims. Even in the 562 nucleotide region where the two sequences overlap, only 503 nucleotides match, which translates to 89.50 percent similarity. Thus, H74302 does not anticipate all the elements of claims 122-126, 129-131 and 135-138 and therefore, is not a 102(b) reference. Hence, this rejection should be withdrawn.

Claims 119-123 and 132-138 are rejected under 35 U.S.C. 102(b) as being anticipated by clones H74303, H58326, H73373 and RO2548 isolated by Hillier *et al.* (1995).

Clone H74303 has 41.73% overall similarity (414 out of 992 nucleotides) to SEQ ID NO: 222, H58326 has 42.14% overall similarity (418 out of 992 nucleotides) to SEQ ID NO: 222, H73373 has 48.39% overall similarity (480 out of 992 nucleotides) to SEQ ID NO: 222 and RO2548 has 38.2% overall similarity (379 out of 992 nucleotides) to SEQ ID NO: 222, defined in the instant claims. Thus, clones H74303, H58326, H73373 and RO2548 do not anticipate the elements of claims 122-126, 129-131 and 135-138 and therefore, are not 102(b) references. Hence, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C55). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: November 3, 2004

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